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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,313	02/12/2008	**Waltraud Bueb**	33613-US-PCT(62106.00023)	9232

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EXAMINER	
KASSA, TIGABU	
ART UNIT	**PAPER NUMBER**
1619	
MAIL DATE	**DELIVERY MODE**
09/15/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,313	BUEB ET AL.	
	Examiner	Art Unit	
	TIGABU KASSA	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *20-24,28 and 30-32* is/are pending in the application.

5a) Of the above claim(s) *28 and 31-32* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *20-24 and 30* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 20-24, 28, and 30-32 are pending. Claims 20-24 and 30 are under consideration in the instant office action. Claims 28 and 31-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a **nonelected species**, there being no allowable generic or linking claims. Claims 1-19, 25-27, 29, and 33-35 are cancelled.

Note: The status of the claims are set forth above based on the claim set filed on September 08, 2011. However, applicant in the response filed on September 08, 2011 in the remarks part applicant indicated that claims 1-19, 25-27, 29 and 33-35 are withdrawn from prosecution which is in contradiction to the status of the claims as filed.

Election/Restrictions

Applicant's election of Group II (claims 20-24, 28 and 30-32) in the reply filed on September 08, 2011 is acknowledged. Furthermore, Applicant's election of the species as lipophilic component a C8-C10 fatty acid monoglycerides or diglycerides or refined glyceroltransesterified corn oil (claim 22) or as an alternative the glyceroltransesterified corn oil as species; as surfactant polyethyleneglycol-hydrogenated castor oil (claim 23); as single species of hydrophilic component propylene glycol (claim 24); and single species of form of composition microemulsion (claim 30) in the reply filed on September 08, 2011 is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement (both in the Group and species election), the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) based on an application filed in United Kingdom application GB 0402679.5 filed on 02/06/04. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on July 20, 2006 is noted and the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the information disclosure statement. A signed copy is attached.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness

Claims 20-24 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang (WO 99/61025) and Gespacher (US Patent No. 6319917, IDS reference).

Applicant Claims

Applicant claims a pharmaceutical composition comprising (4R)-4-[N'-methyl- N'-(3,5-bistrifluoro-methyl-benzoyl) amino]-4-(3,4-dichlorobenzyl)-but-2-enoic acid N- [(R)-epsilon-caprolactam-3-yl]-amide as active agent and a carrier medium comprising a lipophilic component and a surfactant, said composition being in an form that is suitable for oral administration.

Note: The examiner examined the claims with regard to carrier medium limiting the composition claimed above to the elected species of as lipophilic component a C8-C10 fatty acid monoglycerides or diglycerides or refined glyceroltransesterified corn oil (claim 22) or as an

alternative the glyceroltransesterified corn oil as species; as surfactant polyethyleneglycol-hydrogenated castor oil (claim 23); as single species of hydrophilic component propylene glycol (claim 24); and single species of form of composition microemulsion (claim 30)

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Lang teaches on page 9 lines 22-28 as follows:

> In yet another aspect the present invention provides a spontaneously dispersible pharmaceutical composition, preferably in the form of a microemulsion preconcentrate, comprising a piperidine substance P antagonist, e.g. Compound A, and a carrier medium comprising
>
> 1) a hydrophilic phase,
> 2) a lipophilic phase, and
> 3) a surfactant.

Lang specifically teaches a pharmaceutical composition comprising (2R,4S)-N-(1-(3,5-bis(trifluoro- methyl)-benzoyl)-2-(4-chlorobenzyl)-4-piperidinyl)-quinoline-4-carboxamide as active agent and a carrier medium comprising 1) a hydrophilic phase, 2) a lipophilic phase, and 3) a surfactant (see claim 5). Lang specifically teaches on claim 8 a composition as claimed in any preceding claim wherein **the hydrophilic component comprises triethyl citrate or propylene glycol**, **wherein the surfactant comprises a reaction product of a natural or hydrogenated castor oil with ethylene oxide or a polyoxyethylene fatty acid ester**, and **wherein the lipophilic component comprises a transesterified ethoxylated vegetable oil, a C8 to C10 fatty acid mono-, di and/or tri-glyceride, a medium chain fatty acid triglyceride or a refined glycerol-transesterified corn oil**. These teachings meet all of the elected species

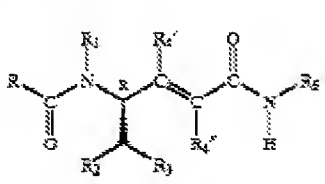
for the lipophilic, surfactant, and hydrophilic components. **Lang specifically teaches on claim 10 that a composition as claimed in any preceding claim in the form of a microemulsion**.

Ascertainment of the Difference between Scope of the Prior Art and the Claims (MPEP §2141.012)

Lang teaches as substance P antagonist a piperidine such as (2R,4S)-N-(1-(3,5-bis(trifluoro- methyl)-benzoyl)-2-(4-chlorobenzyl)-4-piperidinyl)-quinoline-4-carboxamide in its composition. Lang does not specifically teach (4R)-4-[N'-methyl- N'-(3,5-bistrifluoro-methyl-benzoyl) amino]-4-(3,4-dichlorobenzyl)-but-2-enoic acid N- [(R)-epsilon-caprolactam-3-yl]-amide as active agent in its composition. This deficiency is cured by the teachings of Gerspacher.

Gerspacher teaches in the abstract as follows:

Compounds of formula I



(I)

wherein R_1, R_3–R_5, R_4', R_4'' and R_2 are as defined in the description, have valuable pharmaceutical properties and are effective especially as NK1 and NK2 antagonists. They are prepared in a manner known per se.

Gerspacher teaches on column 3, lines 28-53 that the compounds of formula I are effective especially as antagonists of NK1 receptors. Their action on that class of receptors and their action on related receptor systems, for example NK2, render the compounds of formula I

therapeutically useful in the prevention, the treatment or the diagnosis of a number of diseases, for example diseases of the upper and lower respiratory tract, for example bronchial asthma, allergic asthma, etc. **As already mentioned, the compounds of formula I act as antagonists of substance P** (column 3, lines 34-35). The invention relates likewise to pharmaceutical compositions comprising a compound I or a pharmaceutically acceptable salt thereof as active ingredient, and to processes for the manufacture thereof (column 9, lines 3-6). Those pharmaceutical compositions are compositions for enteral, such as oral and also rectal, administration, for parenteral administration, for local administration and especially for administration by inhalation to warm-blooded animals, especially human beings, the compositions comprising the pharmacological active ingredient alone or together with customary pharmaceutical excipients (column 9, lines 6-13). It must be noticed that Gerspacher also teaches that the preparation of (4R)-4-[N'-methyl-N'-(3.5-bistrifluoromethyl-benzoyl)-amino]-4-(3, 4-dichlorobenzyl)-but-2-enoic acid N-[(R)-epsilon-caprolactam-3-yl]-amide which is the P antagonist recited in claim 20 (see example 22) .

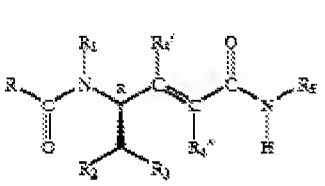
Finding of Prima Facie Obviousness Rationale and Motivation

(MPEP §2142-2143)

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time of the instant invention was made to modify the composition of Lang by substituting the piperidine based P antagonist such as (2R,4S)-N-(1-(3,5-bis(trifluoro- methyl)-benzoyl)-2-(4-chlorobenzyl)-4-piperidinyl)-quinoline-4-carboxamide with the P antagonist (4R)-4-[N'-methyl-N'-(3.5-bistrifluoromethyl-benzoyl)-amino]-4-(3, 4-dichlorobenzyl)-but-2-enoic acid N-[(R)-

epsilon-caprolactam-3-yl]-amide recited in the instant invention because Gerspacher teaches in the abstract as follows:

Compounds of formula I



(I)

wherein R_1, R_2–R_5, R_4', R_4'' and R_6 are as defined in the description, have valuable pharmaceutical properties and are effective especially as NK1 and NK2 antagonists. They are prepared in a manner known per se.

Gerspacher teaches on column 3, lines 28-53 that the compounds of formula I are effective especially as antagonists of NK1 receptors. Their action on that class of receptors and their action on related receptor systems, for example NK2, render the compounds of formula I therapeutically useful in the prevention, the treatment or the diagnosis of a number of diseases, for example diseases of the upper and lower respiratory tract, for example bronchial asthma, allergic asthma, etc. **As already mentioned, the compounds of formula I act as antagonists of substance P** (column 3, lines 34-35). The invention relates likewise to pharmaceutical compositions comprising a compound I or a pharmaceutically acceptable salt thereof as active ingredient, and to processes for the manufacture thereof (column 9, lines 3-6). Those pharmaceutical compositions are compositions for enteral, such as oral and also rectal, administration, for parenteral administration, for local administration and especially for administration by inhalation to warm-blooded animals, especially human beings, the compositions comprising the pharmacological active ingredient alone or together with customary

pharmaceutical excipients (column 9, lines 6-13). It must be noticed that Gerspacher also teaches that the preparation of (4R)-4-[N'-methyl-N'-(3.5-bistrifluoromethyl-benzoyl)-amino]-4-(3, 4-dichlorobenzyl)-but-2-enoic acid N-[(R)-epsilon-caprolactam-3-yl]-amide which is the P antagonist recited in claim 20 (see example 22) .

The skilled artisan would have been motivated to substitute the piperidine based P antagonist taught by Lang with (4R)-4-[N'-methyl-N'-(3.5-bistrifluoromethyl-benzoyl)-amino]-4-(3, 4-dichlorobenzyl)-but-2-enoic acid N-[(R)-epsilon-caprolactam-3-yl]-amide because the two P antagonists are functionally equivalent as P antagonists. It must be known that Lang teaches the remaining required elected species as ingredients in specific embodiment teachings as set forth above. One of ordinary skill in the art would have had a reasonable chance of success in combining the teachings of Lang and Gerspacher because both references teach pharmaceutical compositions containing P antagonists.

In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIGABU KASSA whose telephone number is (571)270-5867. The examiner can normally be reached on 9 am-5 pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Blanchard can be reached on 571-272-0827. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tigabu Kassa 9/10/11

/CHERIE M WOODWARD/
Primary Examiner, Art Unit 1647